REMARKS

Claims 37-39 are pending in the application. Claims 37 and 38 are rejected and claim 39 is allowed.

The amendment to claim 37 adds no new matter. Support for the amendment can be found, *e.g.*, on page 33, lines 1-3.

The previous rejections have been withdrawn and claims 37 and 38 are newly rejected under 35 U.S.C. § 103 as allegedly obvious. This is the only current rejection.

Claims 37 and 38 were rejected as allegedly unpatentable over Bonjouklian, *et al.* (U.S. Patent No. 5,378,725, referred to herein as "Bonjouklian") in view of Arnold, *et al.* (*Genes, Chromosomes, and Cancer* 16:46-54, 1996, referred to herein as "Arnold") and Volinia, *et al.* (*Genomics* 24:472-477, 1994, referred to herein as "Volinia") and further in view of Xiao, *et al.* (*International Journal of Oncology* 6:405-411, 1995, referred to herein as "Xiao") or alternatively, Skorski, *et al.* (*Blood* 86:726-736, 1995, referred to herein as "Skorski"). The Examiner characterizes Bonjouklian as teaching a method of treating PI3 kinase-dependent neoplasms by administering nonpeptide inhibitors of PI3 kinase. The rejection further notes that the catalytic p110 subunit of PI3 kinase is found on chromosome 3q26.3 (Volinia) and that the region 3q26 is amplified (Arnold) in ovarian tumors. Last, she adds that Xiao and Skorski teach that wortmannin suppressed growth of gastric cancer cells and selectively inhibited the proliferation of leukemic cells. The Examiner concludes that it would have been *prima facie* obvious to use the PI3 kinase inhibitor wortmannin to treat any ovarian cancer, including ovarian cancer comprising cells that had regions of chromosome 3q26 amplified. The Examiner also argues that because Volinia teaches that PIK3CA was found in 3q26.3, the ordinary artisan would have been taught that ovarian cancer tumors would include those that had region 3q26 amplified and realized that the method of Bonjouklian would include ovarian tumor that were characterized by the probable amplification of a chromosomal region containing a PI3 kinase. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

As the Examiner knows, in order to establish a proper *prima facie* case of obviousness, the Examiner must establish that there is a suggestion or motivation to modify the

references or to combine the reference teachings; there must be a reasonable expectation of success; and the references or combination of references must teach or suggest all of the claim limitations (*see, e.g.,* MPEP § 2142). The teachings or suggestions to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cr. 1991)). The arguments advanced by the Examiner fail to meet all of these criteria.

First, the combination of references fails to teach or suggest all of the elements of the claimed invention. The references do not teach administration of a PI3 kinase inhibitor to a patient who has an ovarian cancer in which 3q26.3 is determined to be amplified. Although Bonjouklian generally teaches administration of PI3 kinase inhibitors to inhibit cell growth in PI3 kinase-dependent neoplasms, there is no teaching that the patient population to be targeted has an amplification of 3q26.3. Further, Arnold's finding that 3q26 can be amplified in ovarian tumors does not provide the specific element of treatment of a patient population having an amplification at 3q26.3, nor does Volinia's localization of PIK3CA to 3q26.3 provide this element. Accordingly, the references do not disclose all of the elements of the claimed invention.

Second, the Examiner fails to establish that there is a motivation to combine the references. The Examiner argues that because PI3 kinase was localized to 3q26.3, the ordinary artisan would have realized that ovarian tumors having an amplification at 3q26 would have an amplification of PI3 kinase. However, the Examiner does not provide any reasoning as to why one of skill would jump to the conclusion that an amplification of 3q26 would likely result in a PIK3CA-dependent neoplasm. Although Arnold indicates that the region 3q26-qter may contain one or more genes important for tumor initiation and/or progression, there is no suggestion as to the identity of such genes. In fact, Arnold teaches that no candidate oncogenes were known in this region (*see, e.g.,* page 49, last two sentence of column 2).

Next, assuming *arguendo* that there was a motivation to combine the references, there must be a reasonable expectation of success to establish obviousness. The Examiner argues that the teachings of Xiao and Skorski lead one of skill to reasonably expect that PIK3CA kinase inhibitors would be effective against any ovarian cancer cell. However, neither reference

relates to ovarian tumors. Xiao suggests only that PI-3 kinase could be relevant to the oncogenic nature of a human gastric cancer cell line (*see, e.g.*, the last sentence of the abstract, emphasis added); Skorski mere described that PI-3 kinase is involved in the proliferation of certain leukemia cells. Cancer is notoriously heterogeneous, as evidenced by the myriad of scientific publications exploring the mechanism of oncogenesis in many different tumor types. Why would one of skill extrapolate the findings of Xiao. and Skorski to ovarian cancer and conclude that wortmannin would inhibit ovarian cancer cell growth? The Examiner does not provide a proper nexus between the disclosure in these two publications and the likelihood of success in inhibiting ovarian cancer cell growth.

In view of the foregoing, the Examiner has failed to establish a proper case of *prima facie* obviousness. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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